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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/659,097	09/10/2003	Rainer Naeff	CCS-202-CON	4324

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EXAMINER	
KISHORE, GOLLAMUDI S	
ART UNIT	**PAPER NUMBER**
1615	

DATE MAILED: 08/19/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)
	10/659,097	NAEFF ET AL.
	Examiner	Art Unit
	Gollamudi S. Kishore, Ph.D	1615

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 2-14 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 2-14 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

5.02

DETAILED ACTION

Claims included in the prosecution are 2-14.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 2-14 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for single bilayer liposomes, does not reasonably provide enablement for generic, liposomes. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. Liposomes are known in the art as either paucilamellar, multilamellar or unilamellar liposomes. Instant specification discloses as to how to make the single bilayer liposomes (unilamellar), but not other forms of liposomes. There is no adequate support for these liposomes in the specification.

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 2-14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 14 (independent claim) is confusing. Liposomes by nature have an aqueous interior (within the bilayer) and an external aqueous medium. Claim 14 recites an aqueous phase surrounding the liposomes. Does that mean, the liposomes are empty?

'the lecithin' in claim 5, 'the charged electropositive or electronegative lipid compound' in claim 6 and 'the buffer' in claim 7 lack an antecedent basis in the parent claim 14.

It is unclear as to what 'analogous compounds' in claim 11 represents. The examiner suggests the naming of these compounds.

Double Patenting

5. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

6. Claims 2-14 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-10 of U.S. Patent No. 6,645,522. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims in both said patent and instant application are

drawn to the same erythropoietin liposomal compositions. The patented claims although recited as 'product by process' claims, they are still product claims. Instant claims are generic with respect the components making up the liposomes recited in the patented claims. It would have been obvious to one of ordinary skill in the art to prepare liposomes using art well known liposomal components with a reasonable expectation of success.

Claim Rejections - 35 U.S.C. § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 14, 5-7, 10 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over either JP 08 231417 or Maitani in view of Collins (5,874,075) cited above.

9. JP, and Maitani disclose liposomes containing erythropoietin. The liposome lipids include synthetic lecithin and cholesterol and phosphate buffer (note the abstract of JP;

abstract and Experimental section in Maitani). What is lacking in JP and Maitani is the teaching that erythropoietin be on the surface of the liposomes.

Collins as pointed out above, teaches liposomal compositions wherein hematopoietic factors including erythropoietin are attached to the surface of the liposomes. The phospholipids include dipalmitoylphosphatidic acid. The liposomes further contain PEG (stabilizer) and a phosphate buffer. According to Collins, such an attachment stabilizes the proteins such as erythropoietin.

The attachment of erythropoietin on the surface of the liposomes instead of encapsulating it within the liposomes of JP or Maitani would have been obvious to one of ordinary skill in the art since Collins teaches attachment to the surface stabilizes erythropoietin.

10. Claims 3 and 4 are rejected under 35 U.S.C. 103(a) as being unpatentable over either JP 08 231417 or Maitani in view of Collins cited above further in view of JP 61097229.

JP, Maitani and Collins do not teach the inclusion of glycine in the liposomal formulations. Such an inclusion however, would have been obvious to one of ordinary skill in the art in view of JP, which teaches that glycine is a stabilizer for erythropoietin (note the abstract).

11. Claims 2, 8 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over either JP 08 231417 or Maitani in view of Collins cited above, further in view of EP 0253 619 of record.

The teachings of JP, Maitani and Collins have been discussed above. These references however, do not teach the preparation of the liposomes by mixing an ethanolic solution with an aqueous solution and subjecting the mixture to high-pressure homogenization.

EP teaches instant method of preparation of liposomes as applicable to generic 'biologically active agents'. . The method involves the mixing the ethanolic solution and the aqueous medium and subjecting the mixture to high-pressure homogenization (note the examples). EP further teaches that several classical methods of liposomes are known in the art and that the one, which involves injecting the organic solution into an aqueous medium and subjecting the mixture to high-pressure homogenization, is superior. Because no further treatment of the liposomes such as ultra sonication, filtration, centrifugation or dialysis is required prior to use, this process can be used for encapsulating biologically active agents on a large scale suitable for use in pharmaceutical industry. EP further teaches the inclusion of a preservative and an antioxidant (note col. 3, line, 35 through col. 5, line 53 and examples).

The use of the method of preparation of EP for the encapsulation of erythropoietin, with the expectation of obtaining similar encapsulation, would have been obvious to one or ordinary skill in the art since EP teaches the superiority of this method.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gollamudi S. Kishore, Ph.D whose telephone number is

(571) 272-0598. The examiner can normally be reached on 6:30 AM- 4 PM, alternate Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K. Page can be reached on (571) 272-0602. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gollamudi S Kishore, Ph.D
Primary Examiner
Art Unit 1615

GSK